

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 99/01891

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/435 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	ROYET, J. ET AL.: "Notchless encodes a novel WD40-repeat-containing protein that modulates Notch signalling activity" THE EMBO JOURNAL, vol. 17, no. 24, 15 December 1998 (1998-12-15), pages 7351-7360, XP002133042 the whole document ---	1-4, 6-17, 19-25
A	WO 98 20142 A (DALLMAN MARGARET JANE ;HOYNE GERALD FRANCIS (GB); IMPERIAL COLLEGE) 14 May 1998 (1998-05-14) the whole document ---	1-4, 6-17, 19-25
A	WO 97 11716 A (ARTAVANIS TSAKONAS SPYRIDON ;MATSUNO KENJI (US); UNIV YALE (US); F) 3 April 1997 (1997-04-03) page 32, line 35 -page 41, line 36 ---	1-4, 6-17, 19-25
	-/--	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

21 March 2000

Date of mailing of the international search report

14 04 00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Kaas, V

INTERNATIONAL SEARCH REPORT

Interr. 1st Application No

PCT/IB 99/01891

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 97 18822 A (UNIV YALE) 29 May 1997 (1997-05-29)</p> <p>the whole document</p>	<p>1-4, 6-17, 19-25</p>

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 99/01891

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 15
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 5, 18
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/IB 99/01891

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claim 15 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the protein.

Continuation of Box I.1

Claims Nos.: 15

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box I.2

Claims Nos.: 5,18

Claim 5 relates to an extremely large number of possible variants. In fact, the claims contain so many possible alterations of the protein that a lack of clarity and support within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible.

It is not possible to carry out a meaningful search into the state of the art on the basis of claim 18 because its subject-matter is structurally undefined and could not in any event have been functionally tested in the prior art.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB 99/01891

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9820142 A	14-05-1998	AU 4876597 A	29-05-1998
		CZ 9901639 A	13-10-1999
		EP 0942998 A	22-09-1999
		GB 2335194 A	15-09-1999
		NO 992196 A	05-07-1999
		PL 333302 A	22-11-1999
WO 9711716 A	03-04-1997	US 5780300 A	14-07-1998
		AU 7264996 A	17-04-1997
		CA 2233534 A	03-04-1997
		EP 0948348 A	13-10-1999
WO 9718822 A	29-05-1997	AU 1161497 A	11-06-1997
		CA 2238404 A	29-05-1997
		EP 0869802 A	14-10-1998

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB 99/01891

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9820142 A	14-05-1998	AU 4876597 A	29-05-1998
		CZ 9901639 A	13-10-1999
		EP 0942998 A	22-09-1999
		GB 2335194 A	15-09-1999
		NO 992196 A	05-07-1999
		PL 333302 A	22-11-1999
WO 9711716 A	03-04-1997	US 5780300 A	14-07-1998
		AU 7264996 A	17-04-1997
		CA 2233534 A	03-04-1997
		EP 0948348 A	13-10-1999
WO 9718822 A	29-05-1997	AU 1161497 A	11-06-1997
		CA 2238404 A	29-05-1997
		EP 0869802 A	14-10-1998

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 11 July 2000 (11.07.00)	
International application No. PCT/IB99/01891	Applicant's or agent's file reference P020269WO
International filing date (day/month/year) 03 November 1999 (03.11.99)	Priority date (day/month/year) 03 November 1998 (03.11.98)
Applicant COHEN, Stephen et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

31 May 2000 (31.05.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Pascal Piriou Telephone No.: (41-22) 338.83.38
--	--

PATENT COOPERATION TREATY

PCT

REC'D 22 AUG 2000

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference P020269WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/IB99/01891	International filing date (day/month/year) 03/11/1999	Priority date (day/month/year) 03/11/1998
International Patent Classification (IPC) or national classification and IPC C12N15/12		
Applicant EUROPEAN MOLECULAR BIOLOGY LABORATORY et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 31/05/2000	Date of completion of this report 17.08.2000
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Kaas, V Telephone No. +49 89 2399 8704 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IB99/01891

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-30 as originally filed

Claims, No.:

1-25 as originally filed

Drawings, sheets:

1/10-10/10 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. 5, 18.

because:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IB99/01891

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the said claims Nos. 5, 18.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 1-4, 6-17, 19-25
	No: Claims
Inventive step (IS)	Yes: Claims 1-4, 6-17, 19-25
	No: Claims
Industrial applicability (IA)	Yes: Claims 1-4, 6-14, 16, 17, 19-25
	No: Claims 15 (no opinion)

2. Citations and explanations

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

- 1) The WD-40-repeat containing protein having the amino acid sequence of SEQ ID NO: 1 is neither disclosed nor suggested in the prior art which has been found in the International Search Report as a solution to the problem of providing a further modulator of Notch signaling activity. Therefore, insofar the "protein" and "fragment thereof" referred to in claims 1 and 12 to 16 both comprise the sequence referred to as "SEQ ID NO: 1", the said claims would appear to satisfy the criteria as set forth in articles 33(2) and 33(3) PCT. This also applies to dependent claims 2 to 4, 6 to 11 and claims 17 and 19 to 25 which are based on said protein or the nucleotide sequence encoding it.
- 2) A protein fragment which comprises SEQ ID NO:1 is also necessarily a protein. The term "fragment" in claims 1 and 12 to 16 is therefore superfluous. The said claims therefore do not satisfy the criterion set forth in Article 6 PCT (conciseness).
- 3) The term "Notchless mutant" which is used in claim 17 appears to represent an arbitrary designation chosen by the applicant. As such, it does not convey any technical information to the reader of the claim. In absence of any characterizing feature, e.g. a reference either to a specific sequence or to the preceding claims, claim 17 is considered to be unclear (Article 6 PCT).
- 4) For the assessment of present claim 15 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.
- 5) The present report has been established with the assumption that all the claims enjoy the claimed priority date. The P-document cited in the International Search Report has therefore not been considered to be part of the prior art as defined in the regulations (Rule 64(1)-(3) PCT).

From the INTERNATIONAL BUREAU

WMS PCT

**NOTICE INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION TO THE DESIGNATED OFFICES**

(PCT Rule 47.1(c), first sentence)

To:

HALLYBONE, Huw, George
Carpmaels & Ransford
43 Bloomsbury Square
London WC1A 2RA
ROYAUME-UNI

Date of mailing (day/month/year) 11 May 2000 (11.05.00)		
Applicant's or agent's file reference P020269WO		IMPORTANT NOTICE
International application No. PCT/IB99/01891	International filing date (day/month/year) 03 November 1999 (03.11.99)	
Applicant EUROPEAN MOLECULAR BIOLOGY LABORATORY et al		

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
JP,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
CA,EP

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 11 May 2000 (11.05.00) under No. WO 00/26364

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer J. Zahra
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

INTERNATIONAL SEARCH REPORT

International Application No

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☒ Further documents are listed in the continuation of box C.

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Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

8 document member of the same patent family

Date of the actual completion of the international search

21 March 2000

Date of mailing of the international search report

14.04.00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Kaas, V

INTERNATIONAL SEARCH REPORT

Interr. 1st Application No

PCT/IB 99/01891

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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International application No.
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because they relate to subject matter not required to be searched by this Authority, namely:
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2. ☒ Claims Nos.: 5, 18
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
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Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/IB 99/01891

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claim 15 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the protein.

Continuation of Box I.1

Claims Nos.: 15

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box I.2

Claims Nos.: 5,18

Claim 5 relates to an extremely large number of possible variants. In fact, the claims contain so many possible alterations of the protein that a lack of clarity and support within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible.

It is not possible to carry out a meaningful search into the state of the art on the basis of claim 18 because its subject-matter is structurally undefined and could not in any event have been functionally tested in the prior art.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS

If none of the following sub-boxes is used, this sheet should not be included in the request.

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

BOUWMEESTER, Antonius
EUROPEAN MOLECULAR BIOLOGY LABORATORY
POSTFACH 102209
69012 HEIDELBERG
GERMANY

This person is:

- ☐ applicant only
☒ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

NETHERLANDS

State (that is, country) of residence:

GERMANY

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

ROYET, Julien
IBMC
UPR 9022 CNRS
15, RUE RENE DESCARTES
67084 STRASBOURG CEDEX
FRANCE

This person is:

- ☐ applicant only
☒ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

FRANCE

State (that is, country) of residence:

FRANCE

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
☐ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
☐ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

Regional Patent

- ☐ **AP ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☐ **EA Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☐ **OA OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- | | | |
|--|---|---|
| <input type="checkbox"/> AE United Arab Emirates | <input type="checkbox"/> LR Liberia | |
| <input type="checkbox"/> AL Albania | <input type="checkbox"/> LS Lesotho | |
| <input type="checkbox"/> AM Armenia | <input type="checkbox"/> LT Lithuania | |
| <input type="checkbox"/> AT Austria | <input type="checkbox"/> LU Luxembourg | |
| <input type="checkbox"/> AU Australia | <input type="checkbox"/> LV Latvia | |
| <input type="checkbox"/> AZ Azerbaijan | <input type="checkbox"/> MD Republic of Moldova | |
| <input type="checkbox"/> BA Bosnia and Herzegovina | <input type="checkbox"/> MG Madagascar | |
| <input type="checkbox"/> BB Barbados | <input type="checkbox"/> MK The former Yugoslav Republic of Macedonia | |
| <input type="checkbox"/> BG Bulgaria | | |
| <input type="checkbox"/> BR Brazil | <input type="checkbox"/> MN Mongolia | |
| <input type="checkbox"/> BY Belarus | <input type="checkbox"/> MW Malawi | |
| <input checked="" type="checkbox"/> CA Canada | <input type="checkbox"/> MX Mexico | |
| <input type="checkbox"/> CH and LI Switzerland and Liechtenstein | <input type="checkbox"/> NO Norway | |
| <input type="checkbox"/> CN China | <input type="checkbox"/> NZ New Zealand | |
| <input type="checkbox"/> CU Cuba | <input type="checkbox"/> PL Poland | |
| <input type="checkbox"/> CZ Czech Republic | <input type="checkbox"/> PT Portugal | |
| <input type="checkbox"/> DE Germany | <input type="checkbox"/> RO Romania | |
| <input type="checkbox"/> DK Denmark | <input type="checkbox"/> RU Russian Federation | |
| <input type="checkbox"/> EE Estonia | <input type="checkbox"/> SD Sudan | |
| <input type="checkbox"/> ES Spain | <input type="checkbox"/> SE Sweden | |
| <input type="checkbox"/> FI Finland | <input type="checkbox"/> SG Singapore | |
| <input type="checkbox"/> GB United Kingdom | <input type="checkbox"/> SI Slovenia | |
| <input type="checkbox"/> GD Grenada | <input type="checkbox"/> SK Slovakia | |
| <input type="checkbox"/> GE Georgia | <input type="checkbox"/> SL Sierra Leone | |
| <input type="checkbox"/> GH Ghana | <input type="checkbox"/> TJ Tajikistan | |
| <input type="checkbox"/> GM Gambia | <input type="checkbox"/> TM Turkmenistan | |
| <input type="checkbox"/> HR Croatia | <input type="checkbox"/> TR Turkey | |
| <input type="checkbox"/> HU Hungary | <input type="checkbox"/> TT Trinidad and Tobago | |
| <input type="checkbox"/> ID Indonesia | <input type="checkbox"/> UA Ukraine | |
| <input type="checkbox"/> IL Israel | <input type="checkbox"/> UG Uganda | |
| <input type="checkbox"/> IN India | <input checked="" type="checkbox"/> US United States of America | |
| <input type="checkbox"/> IS Iceland | | |
| <input checked="" type="checkbox"/> JP Japan | <input type="checkbox"/> UZ Uzbekistan | |
| <input type="checkbox"/> KE Kenya | <input type="checkbox"/> VN Viet Nam | |
| <input type="checkbox"/> KG Kyrgyzstan | <input type="checkbox"/> YU Yugoslavia | |
| <input type="checkbox"/> KP Democratic People's Republic of Korea | <input type="checkbox"/> ZA South Africa | |
| | <input type="checkbox"/> ZW Zimbabwe | |
| <input type="checkbox"/> KR Republic of Korea | Check-boxes reserved for designating States which have
become party to the PCT after issuance of this sheet: | |
| <input type="checkbox"/> KZ Kazakhstan | <input type="checkbox"/> CR Costa Rica | <input type="checkbox"/> TZ Tanzania |
| <input type="checkbox"/> LC Saint Lucia | <input type="checkbox"/> DM Dominica | |
| <input type="checkbox"/> LK Sri Lanka | | |

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

Box No. VI PRIORITY CLAIM		<input type="checkbox"/> Further priority claims are indicated in the Supplemental Box.		
Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application:* regional Office	international application: receiving Office
item (1) 3/11/98	GB 9824045.0	GB		
item (2)				
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): (1) GB 9824045.0

* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA)
(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA / EP

Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):

Date (day/month/year)

Number

Country (or regional Office)

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following number of sheets:

request : 4
description (excluding sequence listing part) : 30
claims : 3
abstract : 1
drawings : 8
sequence listing part of description : 2

Total number of sheets : 48

This international application is accompanied by the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☒ other (specify): 23/77

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: ENGLISH

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

Anthony James

JAMES, ANTHONY CHRISTOPHER W.P.

HALLYBONE, Huw George

CHECKED

Date: 3-11-99

By: *SCU*

For receiving Office use only		2. Drawings: <input type="checkbox"/> received: <input type="checkbox"/> not received:
1. Date of actual receipt of the purported international application:		
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:		
4. Date of timely receipt of the required corrections under PCT Article 11(2):		
5. International Searching Authority (if two or more are competent): ISA /	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid.	

For International Bureau use only
Date of receipt of the record copy by the International Bureau:

HRE

From the INTERNATIONAL BUREAU

PCT

**NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT**

(PCT Administrative Instructions, Section 411)

To:

HALLYBONE, Huw, George
Carpmeals & Ransford
43 Bloomsbury Square
London WC1A 2RA
ROYAUME-UNI

Date of mailing (day/month/year)
24 March 2000 (24.03.00)

Applicant's or agent's file reference
P020269WO

International application No.
PCT/IB99/01891

International publication date (day/month/year)
Not yet published

IMPORTANT NOTIFICATION

International filing date (day/month/year)
03 November 1999 (03.11.99)

Priority date (day/month/year)
03 November 1998 (03.11.98)

Applicant

EUROPEAN MOLECULAR BIOLOGY LABORATORY et al

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
3. An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document, within a time limit which is reasonable under the circumstances.
4. The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
03 Nove 1998 (03.11.98)	9824045.0	GB	06 Marc 2000 (06.03.00)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

R. Chrem



Telephone No. (41-22) 338.83.38

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

HALLYBONE, Huw G.
CARPMAELS & RANSFORD
43 Bloomsbury Square
London WC1A 2RA
GRANDE BRETAGNE

NOTIFICATION OF RECEIPT
OF DEMAND BY COMPETENT INTERNATIONAL
PRELIMINARY EXAMINING AUTHORITY

(PCT Rules 59.3(e) and 61.1(b), first sentence
and Administrative Instructions, Section 601(a))

Date of mailing
(day/month/year)

2 0. 06. 00

Applicant's or agent's file reference

P020269W0

IMPORTANT NOTIFICATION

International application No.

PCT/IB 99/01891

International filing date (day/month/year)

03/11/1999

Priority date (day/month/year)

03/11/1998

Applicant

EUROPEAN MOLECULAR BIOLOGY LABORATORY et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

31/05/2000

2. This date of receipt is:

- ☒ the actual date of receipt of the demand by this Authority (Rule 61.1(b)).
☐ the actual date of receipt of the demand on behalf of this Authority (Rule 59.3(e)).
☐ the date on which this Authority has, in response to the invitation to correct defects in the demand (Form PCT/IPEA/404), received the required corrections.

3. ☐ **ATTENTION:** That date of receipt is **AFTER** the expiration of 19 months from the priority date. Consequently, the election(s) made in the demand does (do) not have the effect of postponing the entry into the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22). For details, see the *PCT Applicant's Guide*, Volume II.

- ☐ (If applicable) This notification confirms the information given by telephone, facsimile transmission or in person on:

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA/

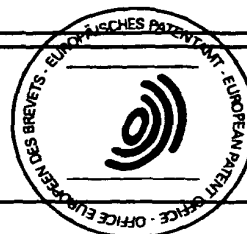


European Patent Office
D-80298 Munich
Tel. (+49-89) 2399-0, Tx: 523656 epmu d
Fax: (+49-89) 2399-4465

Authorized officer

CHAVONAND F H

Tel. (+49-89) 2399-2390



PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

HALLYBONE, Huw G.
CARPMAELS & RANSFORD
43 Bloomsbury Square
London WC1A 2RA
GRANDE BRETAGNE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

WMS

Date of mailing
(day/month/year) 17.08.2000

Applicant's or agent's file reference
P020269WO

IMPORTANT NOTIFICATION

International application No.
PCT/IB99/01891

International filing date (day/month/year)
03/11/1999

Priority date (day/month/year)
03/11/1998

Applicant
EUROPEAN MOLECULAR BIOLOGY LABORATORY et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

 European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Vullo, C

Tel. +49 89 2399-8061



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P020269WO	<div style="display: flex; justify-content: space-between;"> <div> FOR FURTHER ACTION </div> <div> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) </div> </div>	
International application No. PCT/IB99/01891	International filing date (day/month/year) 03/11/1999	Priority date (day/month/year) 03/11/1998
International Patent Classification (IPC) or national classification and IPC C12N15/12		
Applicant EUROPEAN MOLECULAR BIOLOGY LABORATORY et al.		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 4 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application 		
Date of submission of the demand 31/05/2000	Date of completion of this report 17.08.2000	
Name and mailing address of the international preliminary examining authority: <div style="display: flex; align-items: center;"> <div> European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 </div> </div>	Authorized officer Kaas, V Telephone No. +49 89 2399 8704	



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IB99/01891

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-30 as originally filed

Claims, No.:

1-25 as originally filed

Drawings, sheets:

1/10-10/10 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. 5, 18.

because:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IB99/01891

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the said claims Nos. 5, 18.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-4, 6-17, 19-25
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-4, 6-17, 19-25
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-4, 6-14, 16, 17, 19-25
	No:	Claims	15 (no opinion)

2. Citations and explanations

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/IB99/01891

- 1) The WD-40-repeat containing protein having the amino acid sequence of SEQ ID NO: 1 is neither disclosed nor suggested in the prior art which has been found in the International Search Report as a solution to the problem of providing a further modulator of Notch signaling activity. Therefore, insofar the "protein" and "fragment thereof" referred to in claims 1 and 12 to 16 both comprise the sequence referred to as "SEQ ID NO: 1", the said claims would appear to satisfy the criteria as set forth in articles 33(2) and 33(3) PCT. This also applies to dependent claims 2 to 4, 6 to 11 and claims 17 and 19 to 25 which are based on said protein or the nucleotide sequence encoding it.
- 2) A protein fragment which comprises SEQ ID NO:1 is also necessarily a protein. The term "fragment" in claims 1 and 12 to 16 is therefore superfluous. The said claims therefore do not satisfy the criterion set forth in Article 6 PCT (conciseness).
- 3) The term "Notchless mutant" which is used in claim 17 appears to represent an arbitrary designation chosen by the applicant. As such, it does not convey any technical information to the reader of the claim. In absence of any characterizing feature, e.g. a reference either to a specific sequence or to the preceding claims, claim 17 is considered to be unclear (Article 6 PCT).
- 4) For the assessment of present claim 15 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.
- 5) The present report has been established with the assumption that all the claims enjoy the claimed priority date. The P-document cited in the International Search Report has therefore not been considered to be part of the prior art as defined in the regulations (Rule 64(1)-(3) PCT).

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ EP

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only	
Identification of IPEA	Date of receipt of DEMAND
Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION	
Applicant's or agent's file reference P020269WO	
International application No. PCT/IB99/01891	International filing date (day/month/year) 3/11/99
(Earliest) Priority date (day/month/year) 3/11/98	
Title of invention REGULATOR OF NOTCH SIGNALING ACTIVITY	
Box No. II APPLICANT(S)	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)	
EUROPEAN MOLECULAR BIOLOGY LABORATORY POSTFACH 102209 69012 HEIDELBERG DE	
Telephone No.:	
Facsimile No.:	
Teleprinter No.:	
State (that is, country) of nationality: DE	State (that is, country) of residence: DE
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)	
COHEN, Stephen EUROPEAN MOLECULAR BIOLOGY LABORATORY POSTFACH 102209 69012 HEIDELBERG DE	
State (that is, country) of nationality: CA	State (that is, country) of residence: DE
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)	
BOUWMEESTER, Antonius EUROPEAN MOLECULAR BIOLOGY LABORATORY POSTFACH 102209 69012 HEIDELBERG DE	
State (that is, country) of nationality: NL	State (that is, country) of residence: DE
<input checked="" type="checkbox"/> Further applicants are indicated on a continuation sheet.	

Continuation of Box No. II APPLICANT(S)

If none of the following sub-boxes is used, this sheet should not be included in the demand.

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

ROYET, Julien
IBMC
UPR 9022 CNRS
15, RUE RENE DESCARTES
67084 STRASBOURG CEDEX
FRANCE

State (that is, country) of nationality:

FR

State (that is, country) of residence:

FR

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

State (that is, country) of nationality:

State (that is, country) of residence:

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

State (that is, country) of nationality:

State (that is, country) of residence:

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

State (that is, country) of nationality:

State (that is, country) of residence:

☐ Further applicants are indicated on another continuation sheet.

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The following person is ☒ agent ☐ common representative
 and ☐ has been appointed earlier and represents the applicant(s) also for international preliminary examination.
☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.
☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

HALLYBONE, Huw George
 CARPMAELS & RANSFORD
 43 BLOOMSBURY SQUARE
 LONDON WC1A 2RA
 UNITED KINGDOM

Telephone No.:

020-7242 8692

Facsimile No.:

020-7405 4166

Teleprinter No.:

267209

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION**Statement concerning amendments:***

1. The applicant wishes the international preliminary examination to start on the basis of:

☒ the international application as originally filed

the description ☐ as originally filed

☐ as amended under Article 34

the claims ☐ as originally filed

☐ as amended under Article 19 (together with any accompanying statement)

☐ as amended under Article 34

the drawings ☐ as originally filed

☐ as amended under Article 34

2. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.

3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: ENGLISH

☒ which is the language in which the international application was filed.

☐ which is the language of a translation furnished for the purposes of international search.

☐ which is the language of publication of the international application.

☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

Box No. V ELECTION OF STATES

The applicant hereby elects all eligible States *(that is, all States which have been designated and which are bound by Chapter II of the PCT)*

excluding the following States which the applicant wishes not to elect:

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- | | | |
|--|---|--------|
| 1. translation of international application | : | sheets |
| 2. amendments under Article 34 | : | sheets |
| 3. copy (or, where required, translation) of amendments under Article 19 | : | sheets |
| 4. copy (or, where required, translation) of statement under Article 19 | : | sheets |
| 5. letter | : | sheets |
| 6. other (specify) | : | sheets |

For International Preliminary Examining Authority use only

- | received | not received |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |

The demand is also accompanied by the item(s) marked below:

- | | |
|--|---|
| 1. <input checked="" type="checkbox"/> fee calculation sheet | 4. <input type="checkbox"/> statement explaining lack of signature |
| 2. <input type="checkbox"/> separate signed power of attorney | 5. <input type="checkbox"/> nucleotide and or amino acid sequence listing in computer readable form |
| 3. <input type="checkbox"/> copy of general power of attorney; reference number, if any: | 6. <input type="checkbox"/> other (specify): |

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).



MERCER, CHRISTOPHER PAUL
for HALLYBONE, Huw George

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1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply.

☐ The applicant has been informed accordingly.

4. ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.

5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

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Demand received from IPEA on:

PCT

FEE CALCULATION SHEET

Annex to the Demand for international preliminary examination

International application No. PCT/IB99/01891	For International Preliminary Examining Authority use only
Applicant's or agent's file reference P020269WO	Date stamp of the IPEA
Applicant EUROPEAN MOLECULAR BIOLOGY LABORATORY et al	
Calculation of prescribed fees 1. Preliminary examination fee EUR 1,533 P 2. Handling fee (<i>Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.</i>) EUR 147 H 3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box EUR 1,680 <div style="border: 1px solid black; width: 150px; margin-left: 350px; padding: 2px; text-align: center;">TOTAL</div>	
Mode of Payment <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <input checked="" type="checkbox"/> authorization to charge deposit account with the IPEA (see below) <input type="checkbox"/> cheque <input type="checkbox"/> postal money order <input type="checkbox"/> bank draft </div> <div style="width: 45%;"> <input type="checkbox"/> cash <input type="checkbox"/> revenue stamps <input type="checkbox"/> coupons <input type="checkbox"/> other (specify): </div> </div>	
Deposit Account Authorization (<i>this mode of payment may not be available at all IPEAs</i>) The IPEA/ EP <input checked="" type="checkbox"/> is hereby authorized to charge the total fees indicated above to my deposit account. <input checked="" type="checkbox"/> (<i>this check-box may be marked only if the conditions for deposit accounts of the IPEA so permit</i>) is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.	
Deposit Account Number 2805.0059	Date (day/month/year) 31/5/00
Signature Carmaels & Ransford CARPMAELS & RANSFORD	

